

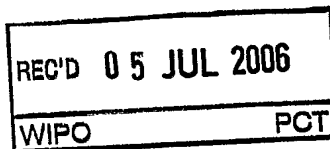
PATENT COOPERATION TREATY


PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)



| | | | | |
|---|--|--|--|--|
| Applicant's or agent's file reference WPP89331 | | FOR FURTHER ACTION | | See Form PCT/IPEA/416 |
| International application No. PCT/EP2005/002250 | | International filing date (day/month/year) 14.02.2005 | | Priority date (day/month/year) 12.02.2004 |
| International Patent Classification (IPC) or national classification and IPC INV. A61K31/4439 A61P35/00 A61P31/16 A61P19/02 | | | | |
| Applicant ISTITUTO SUPERIORE DI SANITA et al | | | | |
| <p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 15 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input checked="" type="checkbox"/> sent to the applicant and to the International Bureau) a total of 2 sheets, as follows:</p> <p><input checked="" type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p> | | | | |
| <p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the report</p> <p><input checked="" type="checkbox"/> Box No. II Priority</p> <p><input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input checked="" type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p> | | | | |
| Date of submission of the demand 13.12.2005 | | Date of completion of this report 30.06.2006 | | |
| Name and mailing address of the international preliminary examining authority:  European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016 | | Authorized officer Langer, O Telephone No. +31 70 340-1972 | | |



**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/EP2005/002250

Box No. I Basis of the report

1. With regard to the **language**, this report is based on
- ☒ the international application in the language in which it was filed
 - ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of:
 - ☐ international search (under Rules 12.3(a) and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4(a))
 - ☐ international preliminary examination (under Rules 55.2(a) and/or 55.3(a))
2. With regard to the **elements*** of the international application, this report is based on (*replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report*):

Description, Pages

1-30 as originally filed

Claims, Numbers

1-24 filed with telefax on 12.12.2005

Drawings, Sheets

1/6-6/6 as originally filed

- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):

* If item 4 applies, some or all of these sheets may be marked "superseded."

**INTERNATIONAL PRELIMINARY REPORT
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Box No. II Priority

1. ☐ This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:
 - ☐ copy of the earlier application whose priority has been claimed (Rule 66.7(a)).
 - ☐ translation of the earlier application whose priority has been claimed (Rule 66.7(b)).
2. ☐ This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rule 64.1). Thus for the purposes of this report, the international filing date indicated above is considered to be the relevant date.
3. Additional observations, if necessary:

see separate sheet

**INTERNATIONAL PRELIMINARY REPORT
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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 10-22; 23, 24 (as far as relating to inventions 1(b), 2-5; and partially 1-9, 23, 24

because:

- ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed (*specify*).
- ☒ no international search report has been established for the said claims Nos. 10-22; 23, 24 (as far as relating to inventions 1(b), 2-5; and partially 1-9, 23, 24
- ☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:
- ☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.
- ☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.
- ☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13*ter*.1(a) or (b) and 13*ter*.2.
- ☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions, and such tables were not available to the International Preliminary Examining Authority in a form and manner acceptable to it.
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.
- ☐ See separate sheet for further details

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Box No. IV Lack of unity of invention

1. ☒ In response to the invitation to restrict or pay additional fees, the applicant has, within the applicable time limit:
- ☐ restricted the claims.
 - ☐ paid additional fees.
 - ☐ paid additional fees under protest and, where applicable, the protest fee.
 - ☐ paid additional fees under protest but the applicable protest fee was not paid.
 - ☒ neither restricted the claims nor paid additional fees.
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is:
- ☐ complied with.
 - ☒ not complied with for the following reasons:
see separate sheet
4. Consequently, this report has been established in respect of the following parts of the international application:
- ☐ all parts.
 - ☒ the parts relating to claims Nos. 1-9, 23 and 24 (as far as part of invention 1(a)) .

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

| | | |
|-------------------------------|-------------|-----------|
| Novelty (N) | Yes: Claims | 1-9,23,24 |
| | No: Claims | |
| Inventive step (IS) | Yes: Claims | |
| | No: Claims | 1-9,23,24 |
| Industrial applicability (IA) | Yes: Claims | 1-9,23,24 |
| | No: Claims | |

2. Citations and explanations (Rule 70.7):

see separate sheet

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30EA/EP.

8.

Re Item II

Priority

The priority with respect to the treatment of diseases other than cancerous conditions appears to be invalid.

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

III.1. Clarity of the claims (Article 6 PCT)

Present claims 1-9, 23 and 24 relate to an extremely large number of possible compounds, namely all proton pump inhibitors, 2-pyridyl methylsulphonyl benzimidazole proton pump inhibitors, antacids and H₂-receptor antagonists.

Support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds claimed.

The definition of the PPIs in claim 4 to be derivatives of 2-pyridyl methylsulphonyl benzimidazole ("2-pyridyl methylsulphonyl benzimidazole proton pump inhibitors") is not sufficiently clear since this expression encompasses a large number of compounds due to the fact that no substituents on the 2-pyridyl methylsulphonyl benzimidazole core have been defined.

The claims further encompass genera of compounds, namely (a) proton pump inhibitors, (b) antacids and (c) H₂-receptor antagonists, defined only by their function wherein the relationship between the structural features of the members of the genus and said function has not been defined. In the absence of such a relationship either disclosed in the as-filed application or recognisable by one skilled in the art based upon information readily available, the skilled artisan would not know how to make and use compounds that lack a structural definition.

In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible.

III.2. An International Search Report has been established for invention 1(a), which is identical to invention 1 as identified in the International Search report, see also item IV. The International Search has been carried out for those parts of the application which relate to invention 1(a) and do appear to be clear, concise, and supported by the description, namely those parts of claims 1-9, 23 and 24 where the PPIs are selected from the group of derivatives of 2-pyridyl methylsulphonyl benzimidazole comprising of omeprazole, lansoprazole, pantoprazole, esomeprazole, and rabeprazole, and where the antacids are selected from the group of compounds consisting of calcium carbonate and the H₂-receptor antagonists ranitidine and cimetidine.

III.3. Since the International Search Report for the present application has been limited to subject-matter as defined in section III.2, this Written Opinion has been established only for invention 1(a) and only for those parts of its subject-matter for which an International Search has been performed, namely those parts that have been specified in section III.2 above.

Re Item IV

Lack of unity of invention (Rule 13 PCT)

IV.1. This Authority considers that there are five (5) inventions covered by the claims indicated as follows:

IV.1.1.

(a) Claims 1-9, and partially 23 and 24

Use of a proton pump inhibitor in the manufacture of a medicament for the treatment of prophylaxis of a cancerous condition, as far as not comprised by sub-invention (b).

(b) Claims 15-17 and partially 10-14 and 20-24

Use of a proton pump inhibitor in combination with at least one further drug indicated against the cancerous condition in the manufacture of a medicament for the treatment of prophylaxis of a cancerous condition.

IV.1.2. Claims 19 and partially 10-14, 18, and 20-24

Use of a proton pump inhibitor in the manufacture of a medicament for combination therapy or prophylaxis of AIDS, wherein the proton pump inhibitor is administered prior

to at least one further drug indicated against AIDS.

IV.1.3. Claims 10-14, 18, 20-24 (all partially)

Use of a proton pump inhibitor in the manufacture of a medicament for combination therapy or prophylaxis of rheumatoid arthritis, wherein the proton pump inhibitor is administered prior to at least one further drug indicated against rheumatoid arthritis.

IV.1.4. Claims 10-14, 18, 20-24 (all partially)

Use of a proton pump inhibitor in the manufacture of a medicament for combination therapy or prophylaxis of ulcerative colitis, wherein the proton pump inhibitor is administered prior to at least one further drug indicated against ulcerative colitis.

IV.1.5. Claims 10-14, 18, 20-24 (all partially)

Use of a proton pump inhibitor in the manufacture of a medicament for combination therapy or prophylaxis of Crohn's disease, wherein the proton pump inhibitor is administered prior to at least one further drug indicated against Crohn's disease.

IV.2. The reasons for which the inventions are not so linked as to form a single general inventive concept, as required by Rule 13.1 PCT, are as follows:

IV.2.1. Problem to be solved

The problem to be solved by the present application resides in the provision of new medicaments and methods for the treatment of (a) a cancerous condition, (b) AIDS, (c) rheumatoid arthritis, (d) ulcerative colitis, and (e) Crohn's disease.

IV.2.2. Solution

The solution for the above problem provided by the present application is to use a proton pump inhibitor (PPI).

IV.2.3. Common technical feature

The compounds of the present application are all proton pump inhibitors. The explicitly named compounds in claims 5, 21 and 23 are 2-pyridyl methylsulphonyl benzimidazole derivatives.

The common technical feature is consequently the use of proton pump inhibitors, in particular of 2-pyridyl methylsulphonyl benzimidazole derivatives for the treatment of a number of various unrelated diseases.

The combination of PPIs with an antacid only appears in claims 1-9.

IV.2.4. Prior art

The document WO-A-97/40039

discloses the use of 2-pyridyl methylsulphonyl benzimidazole derivatives for the treatment of a number of diseases, including gastric cancer (abstract).

The document WO-A-01/44257

discloses the use of proton pump inhibitors for treating or preventing bone disorders, including metastatic bone disease.

The document US5693818

discloses the use of salts of pyridinylmethyl-sulfinyl-1-H-benzimidazoles, in particular the salts of omeprazole, for the "treatment or prophylaxis of inflammatory conditions", including rheumatoid arthritis (column 2, paragraph 2; column 3, paragraph 2).

IV.2.5. Special technical feature (Rule 13.2 PCT)

In view of the disclosure of the prior art document cited above, it appears that the use of PPIs in the treatment of diseases as claimed in the present application, such as cancer and rheumatoid arthritis, is known in the prior art.

The combination of a PPI with an antacid is only claimed for the first invention.

The different diseases are not linked by another technical feature than their alleged involvement in the inhibition of proton pumps.

Both the claimed PPIs and their involvement in (some of) the diseases claimed are known in the prior art, though.

In the present application, no further technical feature(s) can be distinguished that can be regarded as a "special technical feature" involved in the technical relationship among the different inventions.

Consequently, the present application lacks unity of invention, and the different solutions not belonging to a common inventive concept are identified as the different inventions listed above.

After amendment of the claims, present inventions 1(a) and 1(b) appear to be unitary due to the presence of an antacid in the composition.

However, since an International Search Report has been established only for the first invention as identified in the Invitation to Pay Additional Fees (PCT/ISA/206), the sub-inventions 1(a) and 1(b) have been created in order to allow a distinction between searched and unsearched subject-matter within the first invention.

IV.3. Scope of this Written Opinion

An International Search Report has been established for invention 1, sub-invention (a), only. Therefore, this Written Opinion relates only to the subject-matter in relation to this first invention.

No opinion under item V will be given for unsearched subject-matter, i.e. inventions 1(b) and 2-5, see also item III.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

V.1. Scope of this Written Opinion

An International Search Report has been established for invention 1, sub-invention (a), only.

The Reasoned statement with regard to novelty, inventive step or industrial applicability relates only to the subject-matter in relation to this invention 1(a), with a further limitation as defined in section III above.

V.2. Reference is made to the following documents:

- D1: DATABASE WPI Section Ch, Week 200335 Derwent Publications Ltd., London, GB; Class B02, AN 2003-371904 XP002329118 & WO 03/027098 A1 (TAKEDA CHEM IND LTD) 3 April 2003 (2003-04-03)
- D2: EP-A-0 567 643 (YOSHITOMI PHARMACEUTICAL INDUSTRIES, LTD; YOSHITOMI PHARMACEUTICAL) 3 November 1993 (1993-11-03)
- D3: DATABASE WPI Section Ch, Week 200382 Derwent Publications Ltd., London, GB; Class B02, AN 2003-884852 XP002329119 & JP 2003 277262 A (TAKADA K) 2 October 2003 (2003-10-02)
- D4: DATABASE WPI Section Ch, Week 200410 Derwent Publications Ltd., London, GB; Class B02, AN

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International application No.

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- 2004-095264 XP002329120 & KR 2003 072 705 A (KOLON CHEM CO LTD) 19 September 2003 (2003-09-19)
- D5: WO 89/03829 A (AKTIEBOLAGET HAESSLE) 5 May 1989 (1989-05-05)
- D6: US-A-6 015 801 (DAIFOTIS ET AL) 18 January 2000 (2000-01-18)
- D7: WO 02/080917 A (FORSKARPATENT I UPPSALA AB; ENGSTRAND, LARS; HOLMBERG, MARTIN; LARSSON) 17 October 2002 (2002-10-17)
- D8: EP-A-1 306 375 (TAKEDA CHEMICAL INDUSTRIES, LTD) 2 May 2003 (2003-05-02)
- D9: WO 02/13796 A (EBERHARD-KARLS-UNIVERSITAET TUEBINGEN UNIVERSITAETSKLINIKUM; AICHER, W) 21 February 2002 (2002-02-21)
- D10: US-B1-6 489 346 (PHILLIPS JEFFREY OWEN) 3 December 2002 (2002-12-03)
- D11: GRAHAM D Y: "Pancreatic enzyme replacement: the effect of antacids or cimetidine" DIGESTIVE DISEASES AND SCIENCES, PLENUM PUBLISHING CO, US, vol. 27, no. 6, June 1982 (1982-06), pages 485-490, XP002085957 ISSN: 0163-2116
- D12: RAYBURN W ET AL: "ANTACIDS VS. ANTACIDS PLUS NON-PRESCRIPTION RANITIDINE FOR HEARTBURN DURING PREGNANCY" INTERNATIONAL JOURNAL OF GYNECOLOGY AND OBSTETRICS, NEW YORK, NY, US, vol. 66, no. 1, 1999, pages 35-37, XP001122187 ISSN: 0020-7292

V.3. Novelty (Article 33(2) PCT)

The present application, as far as relating to invention 1(a), meets the criteria of Article 33(1) PCT with respect to novelty of the claims under Article 33(2) PCT.

None of the documents in the prior art discloses the combined use of a proton pump inhibitor, the term being limited as indicated under item III, with an antacid, also with the limitation under item III, for the treatment or prophylaxis of a cancerous condition.

Present claims 1-9, 23 and 24, as far as relating to the invention 1(a), appear to be novel in the sense of Article 33(2) PCT.

V.4. Inventive Step (Article 33(3) PCT)

Invention 1(a) of the present application does not meet the criteria of Article 33(1) PCT because the claims 1-9, 23 and 24, as far as relating to this invention, lack inventive step under Article 33(3) PCT.

V.4.1. Problem to be solved

The problem to be solved by invention 1(a) of the present application resides in the provision of an improved medicament for the treatment of a cancerous condition, the medicament being suitably formulated to enhance "the concentration of PPI able to reach the tumor site" (page 6, last paragraph) and to prevent total sequestration of the

PPI in the stomach (claim 6).

The problem to merely treat a cancerous condition is not the problem to be solved by the present invention, since this problem has already been solved and since the role of the antacid, the presence of which distinguishes the present invention from the prior art, is clear from the description, see page 6, last paragraph.

The alleged advantages of the medicament of the present invention, as mentioned on page 2, paragraph 2 of the letter of reply dated 12 December 2005, cannot be identified as parts of the problem to be solved.

V.2.2. Solution

The solution for the above problem provided by the present application is to use a proton pump inhibitor (PPI) in combination with an antacid, such as calcium carbonate or an H₂-receptor antagonist.

V.4.3. Prior art

The document D1 (XP002329118)

discloses the use of acid-stable benzimidazole derivatives that are pro-drugs of the proton pump inhibitor lansoprazole (lansoprazole) for the treatment of various diseases, including gastric cancer and gastric MALT lymphoma (abstract).

The document D2 (EP-A-0567643)

has been cited by the applicant and discloses the use of 2-pyridyl methylsulphonyl benzimidazoles "for the prevention and treatment of tumor" (page 3, line 50 to page 4, line 14; page 9, line 33).

Formula (I) of D2 encompasses the explicitly named compounds of claim 5.

The document D3 (XP002329119)

has been cited by the applicant and discloses a lansoprazole formulation for use as anticancer agent (abstract).

The document D4 (XP002329120)

discloses lansoprazole and omeprazole as anti-tumor drugs (abstract).

The document D5 (WO-A-89/03829)

discloses the use of omeprazole for the treatment of malignant neoplasms (claims 1,4,10,13).

The document D6 (US-6015801)

discloses medicaments comprising histamine H₂ receptor blocker or proton pump inhibitors, including cimetidine, ranitidine, om(e)prazole and lansoprazole, for the treatment of various diseases, including multiple myeloma and metastatic bone disease, involving "tumor-induced skeletal metastases which commonly result from breast cancer, prostate cancer, lung cancer, renal cancer, thyroid cancer, and multiple myeloma" (column 9, lines 53 to column 10, line 3; claims 44, 45, 59).

The document D7 (WO-A-02/080917)

discloses a (weak) activity of lansoprazole against small cell lung cancer (page 4, paragraph 2; figure 5A). The document furthermore discloses the use of PPIs for the treatment or prevention of a multi-drug resistance, such as a condition associated with cancer treatment (abstract).

The document D8 (EP-A-1306375)

discloses the use of salts of lansoprazole for the treatment of gastric cancer (claims 1, 10-13).

The document D9 (WO-A-02/13796)

discloses the use of proton pump inhibitors for the treatment of bone cancer

The document D10 (US-B-6489346)

discloses that the PPIs omeprazole and lansoprazole are "stable at alkaline pH" but that "they are destroyed rapidly as pH falls (e.g. by gastric acid)" (column 7, lines 19 to 30). In order "to protect the PPI against acid degradation" buffering agents, such as calcium carbonate, are used in this document (column 13, line 28 to column 14, line 13). Calcium carbonate is used to make PPI-containing granules (column 16, lines 6-7). The document further discloses that "parietal cell activators", such as calcium carbonate, "enhance the pharmacological activity of the PPI administered" (column 18, paragraph 7).

The document D11 (XP002085957)

discloses that cimetidine is an antacid (Table 1).

The document D12 (XP001122187)

discloses that ranitidine "is marketed as relieving and preventing heartburn and acid ingestion" (page 35, left-hand column, paragraph 1).

Ranitidine and cimetidine are the two H₂-receptor antagonists explicitly mentioned in the present application (last paragraph of page 6).

V.4.5. Difference between the present invention and the closest prior art

Document D1, relating to the treatment of gastric cancer and gastric MALT lymphoma, solves part of the same problem as the present invention, which relates to the treatment of a cancerous condition, and can be considered as representing the closest prior art. The difference between the present application and the closest prior art is the use of a combination of a PPI and an antacid, instead of using an acid-stable PPI prodrug in D1.

V.4.6. Analysis of inventive step

The person skilled in the art, with the knowledge about the need to protect PPIs against premature deactivation by the acids in the stomach, as exemplified by the use of acid-stable prodrugs or enteric coatings in D1, aware of the disclosure of the document D10, in which buffering agents, including calcium carbonate, to "to protect the PPI against acid degradation" are used, would, without the exercise of any inventive skill or activity, consider using buffering agents, such as calcium carbonate, as obvious alternatives to acid-stable prodrugs or enteric coatings in order to solve the problem defined above. It further follows from D11 that cimetidine can be used as an alternative antacid.

The subject-matter of present claims 1-9, and of claims 23 and 24, as far as relating to invention 1(a), lacks inventive step under Article 33(3) PCT.

V.5. Industrial applicability (Article 33(4) PCT)

Present claims 1-9, and claims 23 and 24, as far as relating to invention 1(a), relate to the use of PPIs in the manufacture of a medicament and meet the requirements of Article 33(4) PCT.